09/139,386

WEST

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Term: L7 and (immobiliz$5 or attach$4)

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DATE: Tuesday, September 16, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L8	L7 and (immobiliz$5 or attach$4)	10	L8
L7	(end$1 or termin$3) near5 cleav$3 near5 (phosphorothioate$1 or phosphoramidate) near5 (primer$1 or probe$1 or oligonucleotide$1)	12	L7
L6	(end$1 or termin$3) near5 cleav$3 near5 (phosphorothioate$1 or phosphoraidate$1) near5 primer$1	1	L6
L5	L4 and ((modif$3 near5 base) or (modif$3 near5 sugar) or (modif$3 near5 phosphate backbone))	32	L5
L4	L3 and polymerase chain reaction$1	48	L4
L3	L2 and (end$1 or termi$4)	81	L3
L2	L1 and (immobiliz$5 or attach$4)	82	L2
L1	(phosphorothioate or phosphoramidate)near5(primer$1 or oligonucleotide$1 or probe$1) near5 cleav$4	95	L1

09/139,386

```
=> s (phosphorothioate# or phosphoramidate#)(10a)(end# or termin###)(10a)primer#
L1          17 (PHOSPHOROTHIOATE# OR PHOSPHORAMIDATE#)(10A)(END# OR TERMIN###)(
               10A) PRIMER#

=> s l1 and clea#### and ligand#
L2           0 L1 AND CLEA#### AND LIGAND#

=> s l1 and cleav####
L3           1 L1 AND CLEAV####

=> s l3 and (immobiliz##### or attach### or ligand#)
L4           0 L3 AND (IMMOBILIZ##### OR ATTACH### OR LIGAND#)

=> d l3 bib ab kwic

L3   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS on STN
AN   1996:494192  CAPLUS
DN   125:134793
TI   Synthesis of stereospecific oligonucleotide phosphorothioates and
     antisense oligonucleotides
IN   Tang, Jinyan; Roskey, Allysen M.; Agrawal, Sudhir
PA   Hybridon, Inc., USA
SO   PCT Int. Appl., 37 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 9619572         A1   19960627       WO 1995-US16086  19951212
         W:  AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, FI,
             GB, GE, HU, IS, JP, KE, KG, KP, MD, MG, MK, MN, MW, MX, NO, NZ,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,
             IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,
             NE, SN, TD, TG
     CA 2208528         AA   19960627       CA 1995-2208528  19951212
     AU 9645146         A1   19960710       AU 1996-45146    19951212
     EP 807171          A1   19971119       EP 1995-943748   19951212
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
     CN 1175281         A    19980304       CN 1995-197690   19951212
PRAI US 1994-362631          19941222
     WO 1995-US16086         19951212
AB   Disclosed is a method for synthesizing of stereospecific (Rp)
     phosphorothioate oligonucleotides.  In this method, a primer comprising a
     plurality of deoxyribonucleotides and a ribonucleotide at the 5' terminal
     or 5' penultimate position, is annealed to a template.  The structure is
     contacted with a mixt. of deoxynucleoside .alpha.-triphosphate Sp
     diastereomers and a DNA polymerase to form a PS-Rp oligodeoxynucleotide
     extension which is liberated as a single-stranded PS-Rp oligonucleotide by
     cleavage after the ribonucleotide in the primer.  Also disclosed
     are PS-RP oligonucleotides and oligonucleotides prepd. according to this
     method.
AB   Disclosed is a method for synthesizing of stereospecific (Rp)
     phosphorothioate oligonucleotides.  In this method, a primer comprising a
     plurality of deoxyribonucleotides and a ribonucleotide at the 5' terminal
     or 5' penultimate position, is annealed to a template.  The structure is
     contacted with a mixt. of deoxynucleoside .alpha.-triphosphate Sp
     diastereomers and a DNA polymerase to form a PS-Rp oligodeoxynucleotide
     extension which is liberated as a single-stranded PS-Rp oligonucleotide by
     cleavage after the ribonucleotide in the primer.  Also disclosed
     are PS-RP oligonucleotides and oligonucleotides prepd. according to this
     method.
IT   179312-03-9D, phosphorus-32-end labeled   179312-05-1
```

RL: NUU (Other use, unclassified); USES (Uses)
(**primer**; synthesis of stereospecific oligonucleotide **phosphorothioates** and antisense oligonucleotides)

IT 1310-58-3, Potassium hydroxide, uses 1310-65-2, Lithium hydroxide
1310-73-2, Sodium hydroxide, uses 1336-21-6, Ammonium hydroxide
9026-12-4, Rnase t1 37205-57-5, Rnase u2 37278-25-4, Rnase t2
RL: NUU (Other use, unclassified); USES (Uses)
(template **cleavage** from primer; synthesis of stereospecific oligonucleotide phosphorothioates and antisense oligonucleotides)

```
=> s (phosphorothioate# or phosphoramidate#)(10a)primer#
L5          115 (PHOSPHOROTHIOATE# OR PHOSPHORAMIDATE#)(10A) PRIMER#

=> s l5 and ligand#
L6            2 L5 AND LIGAND#

=> s l6 and cleav####
L7            0 L6 AND CLEAV####

=> s l5 and cleav####
L8           20 L5 AND CLEAV####

=> s l8 and ligand#
L9            0 L8 AND LIGAND#

=> s l8 and (immobiliz##### or attach####)
L10          10 L8 AND (IMMOBILIZ##### OR ATTACH####)

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11          10 DUP REM L10 (0 DUPLICATES REMOVED)

=> d l11 bib ab kwic

L11  ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2003 ACS on STN
AN   2003:196911  CAPLUS
DN   138:232931
TI   Multiplex anchored strand displacement amplification on an electronically
     addressable microchip
IN   Nerenberg, Michael I.; Edman, Carl F.; Westin, Lorelei P.; Feng, Lana L.;
     Landis, Geoffrey C.; Sosnowski, Ronald G.
PA   Nanogen/Becton Dickinson Partnership, USA
SO   U.S., 77 pp.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   US 6531302        B1    20030311      US 1999-290000   19990412
     WO 2000060919     A2    20001019      WO 2000-US9838   20000411
     WO 2000060919     A3    20020103
     WO 2000060919     B1    20020131
         W:  CA, JP, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     JP 2003510012     T2    20030318      JP 2000-610270   20000411
PRAI US 1999-290000    A     19990412
     WO 2000-US9838    W     20000411
AB   Multiplex strand displacement amplification of target nucleic acids using
     primer pair sets that are anchored to electronically addressable capture
     sites on a microarray are described.  The primer pair sets may be
     individually bound to the capture sites or may comprise a unique branched
```

primer pair moiety. The anchored primers allow for the simultaneous multiplex capture, amplification and detection of a target nucleic acid derived from any sample source. The system is also less dependent upon the size of the capture oligonucleotides.

RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Phosphorothioate** oligonucleotides
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(base analog contg., **immobilized**, as **primers**; multiplex anchored strand displacement amplification on electronically addressable microchip)

IT Oligonucleotides
RL: DEV (Device component use); USES (Uses)
(derivs., spacer in primer **immobilization**; multiplex anchored strand displacement amplification on electronically addressable microchip)

IT Primers (nucleic acid)
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(oligonucleotide analog contg., **immobilized**; multiplex anchored strand displacement amplification on electronically addressable microchip)

IT Amino acids, uses
Peptides, uses
Polyoxyalkylenes, uses
RL: DEV (Device component use); USES (Uses)
(spacer in oligonucleotide **immobilization**; multiplex anchored strand displacement amplification on electronically addressable microchip)

IT 81295-06-9, Restriction endonuclease BsoBI 81295-15-0, Restriction endonuclease BstOI 81295-26-3, Restriction endonuclease HphI 81458-03-9, Restriction endonuclease FokI 81811-55-4, Restriction endonuclease HindII 81811-55-4, Restriction endonuclease HincII 82469-86-1, Restriction endonuclease MraI 84522-63-4, Restriction endonuclease Tth111I 86352-30-9, Restriction endonuclease Fnu4HI 87683-74-7, Restriction endonuclease AccI 92228-43-8, Restriction endonuclease BstXI 95076-97-4, Restriction endonuclease NciI 100900-70-7, Restriction endonuclease BsaI 102227-43-0 115630-38-1, Restriction endonuclease BsrI 121855-06-9, Restriction endonuclease MwoI 122007-72-1, Restriction endonuclease BsmI 122319-85-1, Restriction endonuclease PflMI 126469-98-5, Restriction endonuclease BsmAI 135340-86-2, Restriction endonuclease AlwI 172306-44-4, Restriction endonuclease NspI 219575-51-6, Restriction endonuclease BsrBI
RL: ARU (Analytical role, unclassified); CAT (Catalyst use); ANST (Analytical study); USES (Uses)
(**cleavage** site for, in strand displacement amplicons; multiplex anchored strand displacement amplification on electronically addressable microchip)

IT 1173-82-6, DUTP 22003-12-9, 5-Methyl dCTP 29220-54-0, ATP-.alpha.-S 101515-08-6
RL: MSC (Miscellaneous)
(**immobilized** primers contg.; multiplex anchored strand displacement amplification on electronically addressable microchip)

IT 58-85-5, Biotin 9013-20-1, Streptavidin
RL: DEV (Device component use); USES (Uses)
(oligonucleotide **immobilization** using; multiplex anchored strand displacement amplification on electronically addressable microchip)

IT 25322-68-3, Polyethylene glycol
RL: DEV (Device component use); USES (Uses)
(spacer in oligonucleotide **immobilization**; multiplex anchored strand displacement amplification on electronically addressable microchip)

=> d l11 1-10 bib ab kwic

L11 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:196911 CAPLUS
DN 138:232931
TI Multiplex anchored strand displacement amplification on an electronically addressable microchip
IN Nerenberg, Michael I.; Edman, Carl F.; Westin, Lorelei P.; Feng, Lana L.; Landis, Geoffrey C.; Sosnowski, Ronald G.
PA Nanogen/Becton Dickinson Partnership, USA
SO U.S., 77 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6531302	B1	20030311	US 1999-290000	19990412
	WO 2000060919	A2	20001019	WO 2000-US9838	20000411
	WO 2000060919	A3	20020103		
	WO 2000060919	B1	20020131		
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	JP 2003510012	T2	20030318	JP 2000-610270	20000411
PRAI	US 1999-290000	A	19990412		
	WO 2000-US9838	W	20000411		

AB Multiplex strand displacement amplification of target nucleic acids using primer pair sets that are anchored to electronically addressable capture sites on a microarray are described. The primer pair sets may be individually bound to the capture sites or may comprise a unique branched primer pair moiety. The anchored primers allow for the simultaneous multiplex capture, amplification and detection of a target nucleic acid derived from any sample source. The system is also less dependent upon the size of the capture oligonucleotides.
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT **Phosphorothioate** oligonucleotides
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(base analog contg., **immobilized**, as **primers**; multiplex anchored strand displacement amplification on electronically addressable microchip)
IT Oligonucleotides
RL: DEV (Device component use); USES (Uses)
(derivs., spacer in primer **immobilization**; multiplex anchored strand displacement amplification on electronically addressable microchip)
IT Primers (nucleic acid)
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(oligonucleotide analog contg., **immobilized**; multiplex anchored strand displacement amplification on electronically addressable microchip)
IT Amino acids, uses
Peptides, uses
Polyoxyalkylenes, uses
RL: DEV (Device component use); USES (Uses)
(spacer in oligonucleotide **immobilization**; multiplex anchored strand displacement amplification on electronically addressable microchip)
IT 81295-06-9, Restriction endonuclease BsoBI 81295-15-0, Restriction

endonuclease BstOI 81295-26-3, Restriction endonuclease HphI 81458-03-9, Restriction endonuclease FokI 81811-55-4, Restriction endonuclease HindII 81811-55-4, Restriction endonuclease HincII 82469-86-1, Restriction endonuclease MraI 84522-63-4, Restriction endonuclease Tth111I 86352-30-9, Restriction endonuclease Fnu4HI 87683-74-7, Restriction endonuclease AccI 92228-43-8, Restriction endonuclease BstXI 95076-97-4, Restriction endonuclease NciI 100900-70-7, Restriction endonuclease BsaI 102227-43-0 115630-38-1, Restriction endonuclease BsrI 121855-06-9, Restriction endonuclease MwoI 122007-72-1, Restriction endonuclease BsmI 122319-85-1, Restriction endonuclease PflMI 126469-98-5, Restriction endonuclease BsmAI 135340-86-2, Restriction endonuclease AlwI 172306-44-4, Restriction endonuclease NspI 219575-51-6, Restriction endonuclease BsrBI
RL: ARU (Analytical role, unclassified); CAT (Catalyst use); ANST (Analytical study); USES (Uses)
(**cleavage** site for, in strand displacement amplicons; multiplex anchored strand displacement amplification on electronically addressable microchip)

IT 1173-82-6, DUTP 22003-12-9, 5-Methyl dCTP 29220-54-0, ATP-.alpha.-S 101515-08-6
RL: MSC (Miscellaneous)
(**immobilized** primers contg.; multiplex anchored strand displacement amplification on electronically addressable microchip)

IT 58-85-5, Biotin 9013-20-1, Streptavidin
RL: DEV (Device component use); USES (Uses)
(oligonucleotide **immobilization** using; multiplex anchored strand displacement amplification on electronically addressable microchip)

IT 25322-68-3, Polyethylene glycol
RL: DEV (Device component use); USES (Uses)
(spacer in oligonucleotide **immobilization**; multiplex anchored strand displacement amplification on electronically addressable microchip)

L11 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:658292 CAPLUS
DN 137:196646
TI Defined DNA sequences amplifiable with a universal primer pair for use in labeling materials for identification
IN Brown, Tom; Thelwell, Nichola; Maxwell, Paula; Maxwell, Paul; Whiting, Paul
PA Crime Solutions Limited, UK
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002066678	A2	20020829	WO 2002-GB759	20020220
	WO 2002066678	A3	20030530		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2001-4163 A 20010220
AB A method of uniquely identifying an object by labeling it with a DNA sequence is described. The DNA sequence has a terminal region including a

moiety that can be used to **attach** it to a substrate. Adjacent to this is a sequence by which the DNA can be released from the substrate, such as a restriction enzyme **cleavage** site. The remainder of the DNA is the unique identifier that includes a pair of primer binding sites sepd. by a defined and unique DNA sequence. The DNA may also contain base analogs or have a modified backbone that will prevent degrdn. of the label by nucleases. The DNA may also be single-stranded with the **immobilization** region in the loop of a stem loop structure. The partially double stranded region may serve as a primer for an initial amplification. Amplification and sequencing of the unique sequence identifier can be used to demonstrate ownership.

AB A method of uniquely identifying an object by labeling it with a DNA sequence is described. The DNA sequence has a terminal region including a moiety that can be used to **attach** it to a substrate. Adjacent to this is a sequence by which the DNA can be released from the substrate, such as a restriction enzyme **cleavage** site. The remainder of the DNA is the unique identifier that includes a pair of primer binding sites sepd. by a defined and unique DNA sequence. The DNA may also contain base analogs or have a modified backbone that will prevent degrdn. of the label by nucleases. The DNA may also be single-stranded with the **immobilization** region in the loop of a stem loop structure. The partially double stranded region may serve as a primer for an initial amplification. Amplification and sequencing of the unique sequence identifier can be used to demonstrate ownership.

IT DNA
Oligonucleotides
Phosphorothioate oligonucleotides
RL: ANT (Analyte); TEM (Technical or engineered material use); ANST (Analytical study); USES (Uses)
(as identifying labels; defined DNA sequences amplifiable with universal **primer** pair for use in labeling materials for identification)

IT 80498-17-5, Restriction endonuclease EcoRI
RL: CAT (Catalyst use); USES (Uses)
(**cleavage** site for, in oligonucleotide label; defined DNA sequences amplifiable with universal primer pair for use in labeling materials for identification)

IT 57-88-5D, Cholesterol, nucleic acid conjugates 58-85-5D, Biotin, nucleic acid conjugates 1406-18-4D, Vitamin E, nucleic acid conjugates 15181-41-6D, Thiophosphate, nucleic acid conjugates
RL: TEM (Technical or engineered material use); USES (Uses)
(for **immobilization** of oligonucleotide label; defined DNA sequences amplifiable with universal primer pair for use in labeling materials for identification)

L11 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:811995 CAPLUS
DN 137:321241
TI Large-scale sequencing by mass spectrometry of extension products of mass-labeled primers
IN Sampson, Jeffrey R.; Myerson, Joel; Tsalenko, Anna M.; Sampas, Nicholas M.; Webb, Peter G.; Yakhini, Zohar H.
PA Agilent Technologies, Inc., USA
SO Eur. Pat. Appl., 48 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1251136	A2	20021023	EP 2002-252723	20020417
	EP 1251136	A3	20030319		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2002182601 A1 20021205 US 2001-836012 20010417
PRAI US 2001-836012 A 20010417
US 1998-112437 A2 19980709

AB Methods and reagents are disclosed which provide for more sensitive, more accurate and higher through-put analyses of target nucleic acid sequences. The methods and reagents of the present invention may be generically applied to generally any target nucleic acid sequence and do not require a priori information about the presence, location or identity of mutations in the target nucleic acid sequence. The reagents of the invention are mixts. of oligonucleotide precursors having a high level of coverage and mass no. complexity, and also having tags analyzable by mass spectrometry which are covalently linked to the precursors through **cleavable** bonds. A method is also disclosed for analyzing a target nucleic acid sequence employing the mixts. of oligonucleotide precursors having tags analyzable by mass spectrometry covalently linked to the oligonucleotide precursors through **cleavable** bonds, and chem. or enzymic assays to alter the mass of the oligonucleotide precursors prior to mass spectral anal. The enzymic assay may be a polymerase extension assay or a ligation-based assay. The kits for carrying out the methods of the invention are also disclosed.

AB Methods and reagents are disclosed which provide for more sensitive, more accurate and higher through-put analyses of target nucleic acid sequences. The methods and reagents of the present invention may be generically applied to generally any target nucleic acid sequence and do not require a priori information about the presence, location or identity of mutations in the target nucleic acid sequence. The reagents of the invention are mixts. of oligonucleotide precursors having a high level of coverage and mass no. complexity, and also having tags analyzable by mass spectrometry which are covalently linked to the precursors through **cleavable** bonds. A method is also disclosed for analyzing a target nucleic acid sequence employing the mixts. of oligonucleotide precursors having tags analyzable by mass spectrometry covalently linked to the oligonucleotide precursors through **cleavable** bonds, and chem. or enzymic assays to alter the mass of the oligonucleotide precursors prior to mass spectral anal. The enzymic assay may be a polymerase extension assay or a ligation-based assay. The kits for carrying out the methods of the invention are also disclosed.

IT Phosphates, analysis
RL: ARU (Analytical role, unclassified); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent)
(**phosphorothioates**, nucleoside triphosphates contg., in prepn. modified **primer** extension products for mass spectrometry; large-scale sequencing by mass spectrometry of extension products of mass-labeled primers)

IT Linking agents
(photolabile, for **attachment** of mass label to primer; large-scale sequencing by mass spectrometry of extension products of mass-labeled primers)

IT 9012-90-2, DNA polymerase
RL: ARU (Analytical role, unclassified); CAT (Catalyst use); ANST (Analytical study); USES (Uses)
(for **cleavage** of primer extension products in DNA sequencing; large-scale sequencing by mass spectrometry of extension products of mass-labeled primers)

L11 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:656066 CAPLUS
DN 137:164662
TI Mutation analysis by mass spectrometry using photocleavable primers in mutation-dependent primer extension reaction
IN Kostrzewa, Markus; Froehlich, Thomas; Wenzel, Thomas; Jaeschke, Andreas; Hausch, Felix
PA Bruker-Saxonia Analytik G.m.b.H., Germany
SO Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1234888	A2	20020828	EP 2002-2521	20020201
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	DE 10108453	A1	20020912	DE 2001-10108453	20010222
	US 2002187493	A1	20021212	US 2002-79043	20020220
PRAI	DE 2001-10108453	A	20010222		

AB The invention relates to a method of a mass-spectrometric anal. of known mutation sites in the genome, such as single nucleotide polymorphisms (SNPs), using the method of restricted mutation-dependent primer extension. Mutation-dependent primer extension can be carried out simply by using four ddNTPs, such as .alpha.-S-ddNTP. The invention consists of the use of primers with a photocleavable linker, a photocleavable .beta.-cyanoethylphosphoramidites (o-nitrobenzyl derivs.) contg. .alpha. 1,3-propanediol moiety instead of a sugar unit. The photocleavable linker can be used a building block, replacing a regular nucleoside at any position of the primer during primer synthesis. The linker creates a gap in a DNA strand which is almost the same size as a natural DNA building block (nucleoside). The linker forms a bridge over a base pair without inhibiting hybridization or enzymic extension. However, the linker allows the primers to be **cleaved** after extension in order to obtain short DNA fragments which can be more easily detected on the mass spectrometer. The photocleavable linker-tagged primer can also be bonded to a pos. charged group from quaternary ammonium salts to the .alpha.-S-ddNTP terminal positions or to the phosphorothioate nucleoside building blocks. Neutralization of the sugar/thiophosphate backbone by alkylation can increase the detection sensitivity significantly in the mass spectrometric anal. The charge-neutralized variations of the equal-no.-nucleotide primer extension method introduced from these novel compds. within the extension primers enables flexible design of multiplex genotyping reactions. The photocleavable primers can be bonded to a 5' amino group, or biotinylated and bonded to other streptavidin-coated surfaces to facilitate product isolation and purifn.

AB The invention relates to a method of a mass-spectrometric anal. of known mutation sites in the genome, such as single nucleotide polymorphisms (SNPs), using the method of restricted mutation-dependent primer extension. Mutation-dependent primer extension can be carried out simply by using four ddNTPs, such as .alpha.-S-ddNTP. The invention consists of the use of primers with a photocleavable linker, a photocleavable .beta.-cyanoethylphosphoramidites (o-nitrobenzyl derivs.) contg. .alpha. 1,3-propanediol moiety instead of a sugar unit. The photocleavable linker can be used a building block, replacing a regular nucleoside at any position of the primer during primer synthesis. The linker creates a gap in a DNA strand which is almost the same size as a natural DNA building block (nucleoside). The linker forms a bridge over a base pair without inhibiting hybridization or enzymic extension. However, the linker allows the primers to be **cleaved** after extension in order to obtain short DNA fragments which can be more easily detected on the mass spectrometer. The photocleavable linker-tagged primer can also be bonded to a pos. charged group from quaternary ammonium salts to the .alpha.-S-ddNTP terminal positions or to the phosphorothioate nucleoside building blocks. Neutralization of the sugar/thiophosphate backbone by alkylation can increase the detection sensitivity significantly in the mass spectrometric anal. The charge-neutralized variations of the equal-no.-nucleotide primer extension method introduced from these novel compds. within the extension primers enables flexible design of multiplex genotyping reactions. The photocleavable primers can be bonded to a 5' amino group, or biotinylated and bonded to other streptavidin-coated surfaces to facilitate product isolation and purifn.

IT Nucleotides, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(2',3'-dideoxyribo-, triphosphates, .alpha.-S, as terminator; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT Functional groups
(benzyl group, o-nitro, photocleavage site; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT UV radiation
(for photocleavable primer **cleavage**; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT Genotyping (method)
Immobilization, molecular
Mutation
Time-of-flight mass spectrometry
(mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT Primers (nucleic acid)
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT Alkylation
(of sugar/thiophosphate backbone for neutralization, for MALDI mass spectrometry; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT Catalysts
(photochem., photocleavable primer **cleaved** by UV light irradn.; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT Quaternary ammonium compounds, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(photocleavable primer pos. charge group derived from; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT **Phosphorothioate** oligodeoxyribonucleotides
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(photocleavable; mutation anal. by mass spectrometry using photolytically **cleavable primers** in mutation-dependent primer extension reaction)
IT Laser ionization mass spectrometry
(photodesorption, matrix-assisted; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT Laser desorption mass spectrometry
(photoionization, matrix-assisted; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT Amide group
(primer bonded to; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT Nucleic acid amplification (method)
(primer extension, using photocleavable primers; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)

IT Sulfhydryl group
(reactive functional group for covalent linking; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT Genetic polymorphism
(single nucleotide, detection of; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT PCR (polymerase chain reaction)
(using photocleavable primers; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT 3695-85-0
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as mass spectrometry matrix; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT 363626-65-7, 1,3-Propanediol, 1-(2-nitrophenyl)-, bis(dihydrogen phosphate) (ester)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as photocleavable linker in primer; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT 58-85-5, Biotin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(primer labeled with; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT 504-63-2, 1,3-Propanediol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(replacing sugar unit in photocleavable nucleoside; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)
IT 9013-20-1, Streptavidin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(surface coated with, for biotinylated primer **immobilization**; mutation anal. by mass spectrometry using photolytically **cleavable** primers in mutation-dependent primer extension reaction)

L11 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:798467 CAPLUS
DN 135:353694
TI Method for highly parallel analysis of genetic polymorphisms and DNA methylation
IN Berlin, Kurt; Gut, Ivo Glynne
PA Epigenomics A.-G., Germany
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001081620	A2	20011101	WO 2001-DE1607	20010425
	WO 2001081620	A3	20030213		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 10021204 A1 20011108 DE 2000-10021204 20000425
EP 1309728 A2 20030514 EP 2001-942981 20010425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI DE 2000-10021204 A 20000425
WO 2001-DE1607 W 20010425

AB The invention relates to a method for the highly parallel characterization of polymorphisms, esp. SNPs, which can be used for the simultaneous or sep. detection of DNA methylations. A set of probes that is provided with at least one detectable marking characteristic of the corresponding probe is bound to an addressed surface, the bond of the probes to the surface being photochem., chem. or enzymically **cleavable**. A nucleic acid to be analyzed is then bound to said probes, the probes are modified in an allele-specific enzymic reaction and a part of the probes that is irrelevant for the anal. of the allele-specific reaction is removed. The allele-specific products are analyzed by means of the detectable markings and the alleles present in the analyzed nucleic acid probe are detd. Thus, the methylation status of the first methylation position in exon 14 of the factor VIII gene was detd. using MALDI-TOF mass spectrometry. The genomic DNA was first treated with bisulfite then a fragment of exon 14 was amplified with PCR. In the first step of the polymorphism assay, the **primer** TCTATTTACTTCATTCCACTTAAsT*sC (s indicates a **phosphorothioate** linkage; * indicates the presence of a quaternary ammonium group on the T) was extended with DNA polymerase in the presence of the amplicon and .alpha.-S-ddATP and .alpha.-S-ddGTP. Depending on the methylation status of the exon, either TCTATTTACTTCATTCCACTTAAsT*sCsA or TCTATTTACTTCATTCCACTTAAsT*sCsG will be produced. After primer extension, the reaction mixt. was treated with 5'-phosphodiesterase. This produces AsT*sCsA and AsT*sCsG which are reacted with Me iodide then subjected to MALDI-TOF mass spectrometry.

AB The invention relates to a method for the highly parallel characterization of polymorphisms, esp. SNPs, which can be used for the simultaneous or sep. detection of DNA methylations. A set of probes that is provided with at least one detectable marking characteristic of the corresponding probe is bound to an addressed surface, the bond of the probes to the surface being photochem., chem. or enzymically **cleavable**. A nucleic acid to be analyzed is then bound to said probes, the probes are modified in an allele-specific enzymic reaction and a part of the probes that is irrelevant for the anal. of the allele-specific reaction is removed. The allele-specific products are analyzed by means of the detectable markings and the alleles present in the analyzed nucleic acid probe are detd. Thus, the methylation status of the first methylation position in exon 14 of the factor VIII gene was detd. using MALDI-TOF mass spectrometry. The genomic DNA was first treated with bisulfite then a fragment of exon 14 was amplified with PCR. In the first step of the polymorphism assay, the **primer** TCTATTTACTTCATTCCACTTAAsT*sC (s indicates a **phosphorothioate** linkage; * indicates the presence of a quaternary ammonium group on the T) was extended with DNA polymerase in the presence of the amplicon and .alpha.-S-ddATP and .alpha.-S-ddGTP. Depending on the methylation status of the exon, either TCTATTTACTTCATTCCACTTAAsT*sCsA or TCTATTTACTTCATTCCACTTAAsT*sCsG will be produced. After primer extension, the reaction mixt. was treated with 5'-phosphodiesterase. This produces AsT*sCsA and AsT*sCsG which are reacted with Me iodide then subjected to MALDI-TOF mass spectrometry.

ST SNP DNA methylation **immobilized** labeled releasable probe mass spectrometry

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); BPR (Biological process); BSU

(Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(labeled, **immobilized**, releasable; method for highly parallel anal. of genetic polymorphisms and DNA methylation)

IT 4044-65-9, Phenylene-1,4-diisothiocyanate 85419-94-9 134978-97-5 162827-98-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(oligonucleotide **immobilization** and; method for highly parallel anal. of genetic polymorphisms and DNA methylation)

L11 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:655898 CAPLUS
DN 131:282375
TI Improvement of mass resolution and accuracy in screening nucleic acids for polymorphisms by mass spectrometric analysis
IN Monforte, Joseph Albert; Shaler, Thomas Andrew; Tan, Yuping; Becker, Christopher Hank
PA Genetrace Systems Inc., USA
SO U.S., 32 pp., Cont.-in-part of U.S. Ser. No. 715,582.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5965363	A	19991012	US 1996-759993	19961202
	CA 2301875	AA	19980326	CA 1997-2301875	19970919
	WO 9812355	A1	19980326	WO 1997-US17101	19970919
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9745916	A1	19980414	AU 1997-45916	19970919
	US 6566055	B1	20030520	US 1998-89730	19980603
PRAI	US 1996-715582	A2	19960919		
	US 1996-32369P	P	19961202		
	US 1996-759993	A	19961202		
	WO 1997-US17101	W	19970919		

AB This invention relates to methods for screening nucleic acids for polymorphisms by analyzing amplified target nucleic acids using mass spectrometric techniques and to procedures for improving mass resoln. and mass accuracy of these methods of detecting polymorphisms. The methods for improving resoln. and accuracy include (1) reducing the length of the target nucleic acid by removing regions flanking the region of interest and (2) purifn. of single-stranded DNA. Methods for reducing the length include use of PCR primer contg. restriction endonuclease sites. Methods for prepg. single-stranded DNA of required purity include use of PCR primers contg. exonuclease-resistant regions followed by digestion with exonuclease. These same primers may be labeled with a binding pair, such as biotin or streptavidin, which allows **immobilization** of the amplified product. The method was applied to anal. of a tetranucleotide repeat polymorphism in human gene THO1. A biotinylated, 2'-deoxythymidine-5'-(S)-**phosphorothioate**-contg. **primer** was employed. After amplification, the double-stranded DNA was denatured and the target was released by incubation with AgNO3.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB This invention relates to methods for screening nucleic acids for polymorphisms by analyzing amplified target nucleic acids using mass spectrometric techniques and to procedures for improving mass resoln. and

mass accuracy of these methods of detecting polymorphisms. The methods for improving resoln. and accuracy include (1) reducing the length of the target nucleic acid by removing regions flanking the region of interest and (2) purifn. of single-stranded DNA. Methods for reducing the length include use of PCR primer contg. restriction endonuclease sites. Methods for prepg. single-stranded DNA of required purity include use of PCR primers contg. exonuclease-resistant regions followed by digestion with exonuclease. These same primers may be labeled with a binding pair, such as biotin or streptavidin, which allows **immobilization** of the amplified product. The method was applied to anal. of a tetranucleotide repeat polymorphism in human gene THO1. A biotinylated, 2'-deoxythymidine-5'-(S)-**phosphorothioate**-contg. **primer** was employed. After amplification, the double-stranded DNA was denatured and the target was released by incubation with AgNO3.

IT Primers (nucleic acid)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**cleavable**, exonuclease-resistant; improvement of mass resoln. and accuracy in screening nucleic acids for polymorphisms by mass spectrometric anal.)

L11 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:197643 CAPLUS
DN 128:254923
TI Improvement of mass resolution and accuracy in screening nucleic acids for polymorphisms by mass spectrometric analysis
IN Monforte, Joseph Albert; Shaler, Thomas A.; Tan, Yuping; Becker, Christopher H.
PA Genetrace Systems, USA; Monforte, Joseph Albert; Shaler, Thomas A.; Tan, Yuping; Becker, Christopher H.
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9812355	A1	19980326	WO 1997-US17101	19970919
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5965363	A	19991012	US 1996-759993	19961202
	CA 2301875	AA	19980326	CA 1997-2301875	19970919
	AU 9745916	A1	19980414	AU 1997-45916	19970919
PRAI	US 1996-715582	A1	19960919		
	US 1996-32369P	P	19961202		
	US 1996-759993	A1	19961202		
	WO 1997-US17101	W	19970919		

AB This invention relates to methods for screening nucleic acids for polymorphisms by analyzing amplified target nucleic acids using mass spectrometric techniques and to procedures for improving mass resoln. and mass accuracy of these methods of detecting polymorphisms. The methods for improving resoln. and accuracy include (1) reducing the length of the target nucleic acid by removing regions flanking the region of interest and (2) purifn. of single-stranded DNA. Methods for reducing the length include use of PCR primer contg. restriction endonuclease sites. Methods for prepg. single-stranded DNA of required purity include use of PCR primers contg. exonuclease-resistant regions followed by digestion with exonuclease. These same primers may be labeled with a binding pair, such

as biotin or streptavidin, which allows **immobilization** of the amplified product. The method was applied to anal. of a tetranucleotide repeat polymorphism in human gene THO1. A biotinylated, 2'-deoxythymidine-5'-(S)-**phosphorothioate**-contg. **primer** was employed. After amplification, the double-stranded DNA was denatured and the target was released by incubation with AgNO3.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB This invention relates to methods for screening nucleic acids for polymorphisms by analyzing amplified target nucleic acids using mass spectrometric techniques and to procedures for improving mass resoln. and mass accuracy of these methods of detecting polymorphisms. The methods for improving resoln. and accuracy include (1) reducing the length of the target nucleic acid by removing regions flanking the region of interest and (2) purifn. of single-stranded DNA. Methods for reducing the length include use of PCR primer contg. restriction endonuclease sites. Methods for prepg. single-stranded DNA of required purity include use of PCR primers contg. exonuclease-resistant regions followed by digestion with exonuclease. These same primers may be labeled with a binding pair, such as biotin or streptavidin, which allows **immobilization** of the amplified product. The method was applied to anal. of a tetranucleotide repeat polymorphism in human gene THO1. A biotinylated, 2'-deoxythymidine-5'-(S)-**phosphorothioate**-contg. **primer** was employed. After amplification, the double-stranded DNA was denatured and the target was released by incubation with AgNO3.

IT Primers (nucleic acid)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**cleavable**, exonuclease-resistant; improvement of mass resoln. and accuracy in screening nucleic acids for polymorphisms by mass spectrometric anal.)

L11 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:454756 CAPLUS
DN 127:202056
TI Cofactor-assisted self-**cleavage** in DNA libraries with a 3'-'5'-phosphoramidate bond
AU Burmeister, Jens; von Kiedrowski, Gunter; Ellington, Andrew D.
CS Lehrstuhl Organische Chemie I Universitat, Bochum, D-44801, Germany
SO Angewandte Chemie, International Edition in English (1997), 36(12), 1321-1324
CODEN: ACIEAY; ISSN: 0570-0833
PB Wiley-VCH
DT Journal
LA English
AB 3'-5'-Phosphoramidate bond-contg. DNA sequences capable of catalyzing cofactor-assisted self-**cleavage** were obtained by in vitro selection from an oligonucleotide library contg. a randomized 72-mer sequence. The method involved prepn. of **immobilized** phosphoramidate-contg. randomized 72-mer. The 72-mer was then allowed to react in presence of dansylated trimer, hexameric template, and magnesium. Reaction produced a pool of catalytic 72-mers which was amplified for the next round of selection. Neg. selection (removal of those DNA sequences that were released via uncatalyzed hydrolysis) was also utilized. Cloning and sequencing of PCR products from the last rounds revealed a single dominating clone. The secondary structure was predicted and showed tight folding around the const. primer regions. Closer examn. of the cloned sequence showed that it catalyzes the hydrolysis (not transphosphorylation) of an internal 3'-5'-phosphoramidate bond in the presence of a specific trimeric cofactor.
TI Cofactor-assisted self-**cleavage** in DNA libraries with a 3'-'5'-phosphoramidate bond
AB 3'-5'-Phosphoramidate bond-contg. DNA sequences capable of catalyzing cofactor-assisted self-**cleavage** were obtained by in vitro

selection from an oligonucleotide library contg. a randomized 72-mer sequence. The method involved prepn. of **immobilized** phosphoramidate-contg. randomized 72-mer. The 72-mer was then allowed to react in presence of dansylated trimer, hexameric template, and magnesium. Reaction produced a pool of catalytic 72-mers which was amplified for the next round of selection. Neg. selection (removal of those DNA sequences that were released via uncatalyzed hydrolysis) was also utilized. Cloning and sequencing of PCR products from the last rounds revealed a single dominating clone. The secondary structure was predicted and showed tight folding around the const. primer regions. Closer examn. of the cloned sequence showed that it catalyzes the hydrolysis (not transphosphorylation) of an internal 3'-5'-phosphoramidate bond in the presence of a specific trimeric cofactor.

ST self **cleaving** phosphoramidate bond DNA library; deoxyribozyme self **cleaving** phosphoramidate bond

IT Ribozymes
RL: NUU (Other use, unclassified); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(deoxy; in vitro selection and characterization of cofactor-assisted self-**cleaving** phosphoramidate-contg. deoxyribozymes from DNA libraries)

IT Hydrolysis catalysts
Hydrolysis kinetics
Nucleic acid library
(in vitro selection and characterization of cofactor-assisted self-**cleaving** phosphoramidate-contg. deoxyribozymes from DNA libraries)

IT Secondary structure
(predicted; in vitro selection and characterization of cofactor-assisted self-**cleaving** phosphoramidate-contg. deoxyribozymes from DNA libraries)

IT 194555-77-6 194555-78-7
RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(PCR **primer**; in vitro selection and characterization of cofactor-assisted self-**cleaving phosphoramidate** -contg. deoxyribozymes from DNA libraries)

IT 94854-99-6
RL: NUU (Other use, unclassified); USES (Uses)
(hexameric template; in vitro selection and characterization of cofactor-assisted self-**cleaving** phosphoramidate-contg. deoxyribozymes from DNA libraries)

IT 7439-95-4, Magnesium, uses
RL: NUU (Other use, unclassified); USES (Uses)
(in vitro selection and characterization of cofactor-assisted self-**cleaving** phosphoramidate-contg. deoxyribozymes from DNA libraries)

IT 194675-13-3P
RL: NUU (Other use, unclassified); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(in vitro selection and characterization of cofactor-assisted self-**cleaving** phosphoramidate-contg. deoxyribozymes from DNA libraries)

IT 194675-86-0
RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(**phosphoramidate**-contg. PCR **primer**; in vitro selection and characterization of cofactor-assisted self-**cleaving phosphoramidate**-contg. deoxyribozymes from DNA libraries)

IT 194554-76-2, DNA (synthetic 72-nucleotide)
RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(randomized 72-mer library; in vitro selection and characterization of

cofactor-assisted self-**cleaving** phosphoramidate-contg. deoxyribozymes from DNA libraries)

IT 194602-90-9
RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(trimeric cofactor; in vitro selection and characterization of cofactor-assisted self-**cleaving** phosphoramidate-contg. deoxyribozymes from DNA libraries)

L11 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:88765 CAPLUS
DN 126:100252
TI **Cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting
IN Monforte, Joseph Albert; Becker, Christopher Hank; Shaler, Thomas Andrew; Pollart, Daniel Joseph
PA Sri International, USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9637630	A1	19961128	WO 1996-US6116	19960430
	W: AU, CA, CN, JP, KR				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5700642	A	19971223	US 1995-445751	19950522
	US 5830655	A	19981103	US 1996-639363	19960426
	AU 9656352	A1	19961211	AU 1996-56352	19960430
	AU 695705	B2	19980820		
	EP 828855	A1	19980318	EP 1996-913305	19960430
	EP 828855	B1	19991215		
	R: DE, FR, GB, IT, NL				
	JP 11505127	T2	19990518	JP 1996-535680	19960430
	JP 3437184	B2	20030818		
PRAI	US 1995-445751	A	19950522		
	US 1996-639363	A	19960426		
	WO 1996-US6116	W	19960430		

AB The present invention provides modified oligonucleotide primers designed to incorporate a **cleavable** moiety so that a (3') portion of the primer (linked to an extension product) can be released from an upstream (5') portion of the primer. The **cleavable** site may consist of altered internucleoside linkages, e.g. dialkoxysilane, 3'- (or 5'-) S-phosporothioate, 3'- (or 5'-) N-phosphoramidate, or may be uracil or ribose. Upon selective **cleavage** of the **cleavable** site, primer extension products that contain about five or fewer base pairs of the primer sequence are released, to provide more useful sizing and sequence information per fragment than extension products contg. the entire primer. **Cleavage** may be enzymic, with 5'.fwdarw.3'-exonuclease, or chem. The oligonucleotides are sized by mass spectrometry, esp. matrix-assisted laser desorption ionization-time-of-flight mass spectrometry. The oligonucleotide primer may be modified (with a biotin tag, for example) so that it can be **immobilized**. The synthesis of a variety of **cleavable** dinucleotides and their incorporation into oligodeoxynucleotides, **immobilization** of the modified oligodeoxynucleotides, and selective **cleavage** and mass spectral anal. of the products was discussed. The method was applied to detection of point mutations in a model target sequence.

TI **Cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting

AB The present invention provides modified oligonucleotide primers designed

to incorporate a **cleavable** moiety so that a (3') portion of the primer (linked to an extension product) can be released from an upstream (5') portion of the primer. The **cleavable** site may consist of altered internucleoside linkages, e.g. dialkoxysilane, 3'- (or 5'-) S-phosporothioate, 3'- (or 5'-) N-phosphoramidate, or may be uracil or ribose. Upon selective **cleavage** of the **cleavable** site, primer extension products that contain about five or fewer base pairs of the primer sequence are released, to provide more useful sizing and sequence information per fragment than extension products contg. the entire primer. **Cleavage** may be enzymic, with 5'.fwdarw.3'-exonuclease, or chem. The oligonucleotides are sized by mass spectrometry, esp. matrix-assisted laser desorption ionization-time-of-flight mass spectrometry. The oligonucleotide primer may be modified (with a biotin tag, for example) so that it can be **immobilized**. The synthesis of a variety of **cleavable** dinucleotides and their incorporation into oligodeoxynucleotides, **immobilization** of the modified oligodeoxynucleotides, and selective **cleavage** and mass spectral anal. of the products was discussed. The method was applied to detection of point mutations in a model target sequence.

ST oligonucleotide **cleavable** sizing mass spectrometry; DNA sequence detn mass spectrometry; single base DNA fingerprinting mass spectrometry

IT Genetic methods
(adenine fingerprinting of DNA; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT Nucleotides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**cleavable** linkage; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT DNA sequence analysis
Mass spectrometry
Time-of-flight mass spectrometry
(**cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT Primers (nucleic acid)
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT **Immobilization**, biochemical
(of primers; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT Laser ionization mass spectrometry
(photodesorption, matrix-assisted; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT Laser desorption mass spectrometry
(photoionization, matrix-assisted; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT Genetic methods
(single base DNA fingerprinting; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT Oligodeoxyribonucleotides
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(single dialkoxysilane linkage-contg.; **cleavable** primers and

oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT Oligodeoxyribonucleotides
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(single **phosphoramidate** linkage-contg.; **cleavable primers** and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT Oligodeoxyribonucleotides
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(single thiophosphate linkage-contg.; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT 50-69-1, Ribose 66-22-8, Uracil, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**cleavable** linkage; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT 185831-49-6D, biotin conjugate
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**cleavable** primer; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT 185831-48-5
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(**cleavable** primer; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT 79121-99-6, 5'.fwdarw.3'-Exonuclease
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT 1173-82-6, DUTP 59088-21-0, Uracil DNA-glycosylase
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(in adenine fingerprinting; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

IT 9012-90-2, DNA polymerase 9015-85-4, DNA ligase
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer extension with; **cleavable** primers and oligonucleotide sizing by mass spectrometry and application to DNA sequencing and single base fingerprinting)

L11 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:2245 CAPLUS
DN 120:2245
TI Automated sequencing of large fragments of DNA using bases labelled with **cleavable** reporter groups
IN Rosenthal, Andre; Brenner, Sydney
PA Medical Research Council, UK
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9321340 A1 19931028 WO 1993-GB848 19930422
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9340208 A1 19931118 AU 1993-40208 19930422
EP 640146 A1 19950301 EP 1993-909381 19930422
EP 640146 B1 19971029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
JP 07507681 T2 19950831 JP 1993-518158 19930422
AT 159766 E 19971115 AT 1993-909381 19930422
ES 2110604 T3 19980216 ES 1993-909381 19930422
US 6087095 A 20000711 US 1994-325224 19941209
PRAI GB 1992-8733 A 19920422
WO 1993-GB848 A 19930422

AB A primer extension method for sequencing DNA that involves directly testing the incorporation of different bases is described. The testing is carried out using a **cleavable** reporter group and the sugar phosphate may also be blocked with a **cleavable** group to prevent secondary incorporation; other forms of inhibition of chain elongation may also be used. The sample is incubated in turn with single labeled nucleotides and any incorporation is measured and the incorporated base is then removed or deprotected and the next base is detd. Removal of the labeled and blocked base may be carried out with exonuclease III in which case the 3'-terminal base of the **primer** is linked with an exonuclease resistant bond such as a **phosphorothioate**. Several variants of the method are described and demonstrated.

TI Automated sequencing of large fragments of DNA using bases labelled with **cleavable** reporter groups

AB A primer extension method for sequencing DNA that involves directly testing the incorporation of different bases is described. The testing is carried out using a **cleavable** reporter group and the sugar phosphate may also be blocked with a **cleavable** group to prevent secondary incorporation; other forms of inhibition of chain elongation may also be used. The sample is incubated in turn with single labeled nucleotides and any incorporation is measured and the incorporated base is then removed or deprotected and the next base is detd. Removal of the labeled and blocked base may be carried out with exonuclease III in which case the 3'-terminal base of the **primer** is linked with an exonuclease resistant bond such as a **phosphorothioate**. Several variants of the method are described and demonstrated.

IT Deoxyribonucleic acids
RL: BIOL (Biological study)
(**immobilized**, sequence detn. by sequential testing of incorporation of labeled bases in primer extension of)

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